The Intercontinental Journal of
Emergency Medicine

Case Report

DOI: 10.51271/ICJEM-0010

Can mRNA vaccine against COVID-19 cause pancytopenia?

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Cite this article: Hamieh C, El Hussein M, Zahereddine Y, Revue E. Can mRNA vaccine against COVID-19 cause pancytopenia?. *Intercont J Emerg Med.* 2023;1(2):34-36.

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Received: 03/06/2023 ◆ **Accepted**: 28/06/2023 ◆ **Published**: 30/06/2023

ABSTRACT

COVID-19 pandemic changed the world. The fight against acquiring this virus went from social distancing, lockdowns and wearing masks, to mass vaccinations. Several vaccines invaded the market, and nations raced towards vaccinating all the population in order to reach herald immunity. mRNA vaccine is one of the most commonly used vaccine nowadays, and although it has a very high efficacy rate, many side effects were reported. A previously healthy young woman presented to our hospital, 1 week after receiving her first COVID-19 mRNA vaccine due severe aphthous ulcers, fatigue and fever. The patient was found to have pancytopenia. Although several side effects were reported to all the COVID-19 vaccines, pancytopenia is not one of the most commonly reported side effects in the literature. In this case report, we talk about is mentioned in the literature, the clinical picture of this patient, the evolution during her hospitalization, and the outcome.

Keywords: COVID-19, SARS-COV-2, pancytopenia, vaccine, mRNA vaccine, side effects

INTRODUCTION

The novel coronavirus has been identified in 2019 after its massive spread in China. After causing acute medical conditions and high death rates in several countries, the World Health Organization (WHO) considered the Corona Virus Disease 2019 (COVID-19) as a pandemic in March 2020.[1] Moreover, several policies have been imposed in order to hinder the spread of the virus. Each country had its own, such as social distancing, mandatory wear of masks, total or partial lockdowns, and developing medicinal remedies. Rapidly, vaccines were developed and introduced to the market worldwide. Different companies and countries were involved and at least 5 brands are currently available.[2] After roughly one year, The United States Food and Drug Administration (FDA) approved the urgent use of the mRNA vaccine with a minimum 21-day period between the first and the second doses 3. Subsequently, a large and a growing body of literature has recognized the common side effects following the administration of the vaccine.[3-6]

In a study conducted among healthcare workers in the Czech Republic, have identified injection site pain as the most common side effect, followed by fatigue, headache, and muscle pain.[4] Moreover, the majority of these side effects have lasted 1 to 3 days.[4] A more comprehensive description was proposed by El-Shitany et al. who investigated side effects after the first dose and the second dose separately. Adverse events were more prevalent after the second dose, these included injection site pain, flu-like symptoms, and hypersensitivity reactions such as tachycardia and dyspnea.[3] Furthermore, the center of disease control (CDC) has identified 47 cases of anaphylaxis following the administration of mRNA vaccine and in most cases, patients received urgent care.[5]

A lot of less prevalent symptoms and reactions were reported in the literature, some including gastrointestinal, hematologic, musculoskeletal and neurologic.[6] In this article we present the case of a previously healthy female who presented to the emergency department with pancytopenia post the first shot of mRNA COVID-19 vaccine.

CASE

A 31year-old female patient presented to the emergency department of our university medical center with fatigue, low grade fever, aphthous ulcers and subsequently decreased oral intake. Patient reports that symptoms began 6 days prior to presentation, started with generalized fatigue, a fever of Tmax 38 degree Celsius, and a progressive eruption of painful oral ulcers, disabling her from tolerating food intake. Symptoms were not associated with any genitourinary symptoms, gastrointestinal or respiratory symptoms. Patient is previously healthy, with no significant social history, does not smoke nor consumes illicit drugs or alcohol. She denied any food or drug allergies and her family history is negative for rheumatologic disorders, immunodeficiency or autoimmune diseases.

To note that the patient had received her first dose of mRNA COVID-19 vaccine 24 hours prior to the initiation of her symptoms.

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On bedside exam, patient was ill-looking, in distress and pale. Cardio-pulmonary exam was normal; abdomen was soft and non-tender. Extremities showed mild skin dryness, but peripheral pulses were palpated, and no edema or rash was detected. However, she had multiple erosive ulcers of the buccal mucosa, not involving the lips nor the perioral area. Vaginal exam was not done but patient denied any itchiness or ulcers. Her blood pressure, heart rate and oxygen saturation were within normal range and her temperature in the emergency department was 37.8 degree Celsius. The patient's blood tests showed decrease in the counts of all the hematopoietic lineage (**Table 1**). Other findings were sodium of 134 mEq/L, potassium 3.4 mEq/L, chlore 101 mEq/L, bicarbonate 17 mEq/L. Liver enzymes were all normal, lactic acid was normal and C-reactive protein was 3.8 mg/dl (elevated). Patient was admitted for further evaluation.

During her stay, blood test to identify causes of pancytopenia were conducted. For instance, HIV 1 and 2 testing came out negative, serology for herpes virus 1&2, and parvovirus B19 were also negative along with, ANA, Tzanc smear, blood cultures and cultures from the oral ulcers and mucosa. Patient was not malnourished; her BMI was above 20 kg/m² with normal albumin blood levels; and there was no family history of similar disorder. No exposure to chemicals or recent medicine was noted in the personal history.

Furthermore, her complete blood count was daily repeated and showed improvement within two days, as described in **Table 1**. Her management consisted of conservative, supportive measures such as daily oral proton pump inhibitor, anti-pyretics, xylocaine topical for oral ulcer, repetitive mouth washes, intravenous hydration, and later was started on itraconazole 200 mg daily to cover for possible oral fungal infection. Nevertheless, 72 hours later, no improvement in the patient's clinical status was observed and especially concerning her oral ulcers and tolerance of oral intake, and little increase was noted on the blood exams. Patient was diagnosed with transient pancytopenia secondary to the vaccine against COVID-19 infection.

On her routine checkup 6 months later the patient had recovered clinically with normal complete blood count.

DISCUSSION

In this case, a previously healthy young female presented with decrease in number of all hematopoietic cell lineage and diffuse oral ulcers. The reference range for hemoglobin, white blood count (WBC) and platelets differ among laboratories, standard values were issued by the WHO: Hemoglobin < 12 gm/dL for non-pregnant women, WBC < 1800 × 10^9/L, and platelets <150,000 10^9/L.[7] For this patient, no biological or metabolic cause was identified, and symptoms were thought to be related to COVID-19 mRNA vaccine. In fact, it is not new to point out pancytopenia as a vaccine side effect. Measles, mumps and rubella vaccine, which is mandatory for children, has been shown to cause bone marrow aplasia in cases as reported by Manoochehr Mahram.[8] It was also seen post hepatitis B vaccine.[9] On the other hand, physicians have identified pancytopenia as one of the adverse events of infection with COVID-19 virus, Yi Zaho et al.[10] presented a case where a 69-year-old male patient suffering from Corona Disease had pancytopenia, where platelet count was the first to normalize with supporting care. A similar case was discussed by Bridwell et al.[11] where the patient required multiple transfusions. Likewise, in our case, the vaccinated patient showed rapid improvement of platelet count first, and slower recovery of hemoglobin and leukocytes. Therefore, it is not out of the norm for patient vaccinated with messenger RNA to have pancytopenia.

Furthermore, this patient presented with severe oral ulcers, which usually are a manifestation of viral infections such as herpes or autoimmune disorders such as Behçet. Nevertheless, our patients ANA and viral panel were negative. In addition, a large retrospective study that targeted the side effects of different COVID-19 vaccine, including mRNA, showed that of the 922 participants, 14% had oral ulcers, and 36% had oral blisters both of which seen in our patient.[3]

Finally, COVID-19 could also be a trigger for autoimmune disorders. Two cases of Goiter were described in the literature post vaccination against COVID-19, and as per the authors, they both met the diagnostic criteria for autoimmune/inflammatory syndrome induced by adjuvants (ASIA), which in their cases and our case is the vaccine.[12] Giving the fact that this patient improved on colchicine, her presentation can be linked to an underlying autoimmune disorder suppressing her bone marrow, triggered by the vaccine. The hypothesis could not be clear whether the vaccine triggered a hidden autoimmune disease, or the pancytopenia and oral ulcers are separate side effects of mRNA vaccine.

CONCLUSION

This female patient received the first dose of COVID-19 mRNA vaccine and few days later, she started complaining of fatigue explained by pancytopenia and eruption of oral

Table 1. CBCD trend during the hospitalization

CBCD	Ref Range	Units	09/08/21	08/08/21	07/08/21 Day 1 post Colchicine	06/08/21	05/08/21	04/08/21
			OK	OK	OK	OK	OK	
WBC	5.2-12.4	x10^3/µL	3.29	4.17	4.32	3.86	3.48	3.52
RBC	4.2-5.4	x10?/µL	4.61	4.56	4.32	4.01	3.66	4.09
HGB	12-16	g/dL	11.9	11.8	11.6	10.6	10.1	10.9
HCT	34-47	%	38.4	38.3	36.0	34.0	31.2	34.7
MCV	81-99	fL	83.2	83.9	83.4	84.7	85.2	84.7
MCH	27-31	pg	25.9	25.9	26.8	26.5	27.7	26.5
MCHC	32-37	g/dL	31.1	30.9	32.1	31.3	32.5	31.3
CHCM	32-37	g/dL	30.6	30.6	30.2	29.7	30.2	30.1
RDW	11.5-14.5	%	14.1	14.6	14.3	14.2	14.9	14.7
HDW	2.2-3.2	g/dL	3.29	3.32	3.27	3.09	3.07	3.13
PLT	150-400	x10^3/µL	211	195	151	113	100	109

lesions. With the negative social and family history and non-significant blood tests, viral serology, nutritional assessment, blood and wound cultures workup, the whole picture was identified as triggered by the vaccine but nevertheless no correlation can be surely identified. The patient however could have benefited from a whole autoimmune workup, as the ANA alone is not 100% sensitive nor specific. The physicians could have also pushed the investigations further, to include a dental checkup, lesion biopsy and bone marrow analysis. A time window after which symptoms can be related to the vaccine is also not specified in the literature; closer observations and broader studies and data collections should be made.

ETHICAL DECLARATIONS

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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